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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/824,321	04/12/2004	Andre Rosowsky	56369 (70157)	5857

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EXAMINER	
BALASUBRAMANIAN, VENKATARAMAN	

ART UNIT	PAPER NUMBER
1624	

DATE MAILED: 09/29/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/824,321	ROSOWSKY ET AL.	
	Examiner	Art Unit	
	Venkataraman Balasubramanian	1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *11 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *38,39,41-49 and 55* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *38,39 and 41-43* is/are allowed.

6)☒ Claim(s) *44-49 and 55* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' response, which included cancellation of claim 40 and amendment to claims 39 and 41-43, filed on 9/11/2006, is made of record. Claims 38, 39, 41-49 and 55 are now pending.

In view of applicants' response, all 112 rejections and prior art rejections made in the previous office action have been deemed as obviated.

However, upon further consideration, the Finality of the previous office action is withdrawn to apply the following rejections.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 47 and 49 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 47 is indefinite as it recites, "any claim 44".

2. Claim 49 lacks antecedent basis as it recites "parasitic infection". Claim 44 on which claim 49 is dependent does not recite parasitic infection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 44-55 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating pneumonia caused by Pneumocystis carinii infection, does not reasonably provide enablement for who are those mammals susceptible to by Pneumocystis carinii infection and enablement for such infection in any or all immuno-compromised mammal and those with any or all autoimmune disorder generically embraced in claim 44 including those specifically recited in claims 45 and 48. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. Following reasons apply.

The instant claim 44 and its dependent claims 45-49 and 55 are drawn to "treating a mammal suffering from or susceptible to Pneumocystis carinii infection" while the scope claim 45-49 and 55 are drawn to treating immuno-compromised mammal with or without autoimmune disorder. Claims 44-49 and 55 are reach through claims. Reach through claims , in general have a format drawn to mechanistic, receptor binding or enzymatic functionality and thereby reach through any or all diseases, disorders or conditions for which they lack written description and enabling disclosure in the specification.

In the instant case, because of the inhibition of DHFR enzyme by the instant compounds, it is recited that instant compounds, besides treating HIV patient who have opportunistic Pneumocystis carinii infection, are useful for treating immune-compromised mammal with or without autoimmune disorder, for which there is no adequate written description and enabling disclosure in the instant specification. More specifically because HIV patients have opportunistic Pneumocystis carinii infection , it

based on that finding the claim reach through any or all immune compromised mammals or those with autoimmune disorder or disease without providing any support in the specification that all immune-compromised mammals would have opportunistic Pneumocystis carinii infection. Prior art search in the related area also does not support the notion any immune compromised mammal or those with autoimmune disorder or disease would necessarily have Pneumocystis carinii infection. In fact every mammal is susceptible to bacterial infection and it is not clear how would know who would be specifically susceptible to Pneumocystis carinii infection.

In addition, the scope of these claims include mammal susceptible to Pneumocystis carinii infection. As recited it scope appears to include prophylaxis of Pneumocystis carinii infection which is not adequately enabled solely based on the activity of the compounds provided in the specification.

The term " prophylaxis" actually means to prevent spread of a disease (as per Meriam Webster's Dictionary) and there is no disclosure as to how one skilled in the art can reasonably establish the basis and the type of subject to which the instant compounds can be administered in order to have the "prevention" effect. There is no evidence of record, which would enable the skilled artisan in the identification of the people who have the potential of becoming afflicted with the disease(s) or disorder(s) claimed herein.

No compound has ever been found to prevent bacterial infection generally and Pneumocystis carinii infection. Since this assertion is contrary to what is known in medicine, proof must be provided that this revolutionary assertion has merits. The

existence of such a "compound" is contrary to our present understanding of modern medicine. Thus, it is beyond the skill of clinician today to get an agent to be effective against bacterial infection including Pneumocystis carinii infection.

Note substantiation of utility and its scope is required when utility is "speculative", "sufficiently unusual" or not provided. See Ex parte Jovanovics, 211 USPQ 907, 909; In re Langer 183 USPQ 288. Also note Hoffman v. Klaus 9 USPQ 2d 1657 and Ex parte Powers 220 USPQ 925 regarding type of testing needed to support in vivo uses.

Next, applicant's attention is drawn to the Revised Utility and Written Description Guidelines, at 66 FR 1090-1099, 2001 wherein it is emphasized that 'a claimed invention must have a specific and substantial utility'. The disclosure in the instant case is not sufficient to enable the instantly claimed method of preventing solely based on the inhibitory activity disclosed for the compounds. The state of the art is indicative of the requirement for undue experimentation. See Snyder et al., J. Med. Liban 48(4): 208-214, 2000 (PubMed Abstract provided), wherein with regards to antibacterial therapies, it is stated that " common bacteria whose susceptibility to antimicrobials is no longer predictable". Note also that despite the fact there are several commercial antibacterial agents are available, it is still difficult to treat several pathogens such as those cause leprosy, meningitis, sexually transmitted infections, anthrax etc.

In evaluating the enablement question, several factors are to be considered. Note *In re Wands*, 8 USPQ2d 1400 and *Ex parte Forman*, 230 USPQ 546. The factors include: 1) The nature of the invention, 2) the state of the prior art, 3) the predictability or lack thereof in the art, 4) the amount of direction or guidance present, 5) the presence

or absence of working examples, 6) the breadth of the claims, and 7) the quantity of experimentation needed.

1) The nature of the invention: Therapeutic and prophylactic use of the compounds in treating Pneumocystis carinii infection that require DHFR inhibiting activity of instant compound and finding those who would be susceptible to the said infection and general treatment of any or all immune-comprised mammal or those suffering from any or all autoimmune disease or disorder.

2) The state of the prior art: Although there are large number DHFR inhibiting agents, none of them are claimed or shown to be useful in preventing any or all parasitic infections including Pneumocystis carinii infection.

3) The predictability or lack thereof in the art: Applicants have not provided any competent evidence or disclosed tests that are highly predictive for the pharmaceutical use of the instant compounds for treating any or all parasitic infections. Pharmacological activity in general is a very unpredictable area. Note that in cases involving physiological activity such as the instant case, "the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved". See *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

4) The amount of direction or guidance present and 5) the presence or absence of working examples: Specification has no working examples for preventing Pneumocystis carinii infection and identifying who would be in need of or who will be susceptible. There is no teaching that all immune comprised mammals or those with autoimmune disease or disorder would be susceptible Pneumocystis carinii infection. In fact,

specification has no testing of any of the compounds of the instant claim 39 and the state of the art is that the effects of bacterial agents based on the disclosed inhibitory activity are unpredictable and at best limited to treating bacterial infections.

6) The breadth of the claims: The instant claims embrace any or all parasitic infections including those yet to be related to DHFR activity.

7) The quantity of experimentation needed would be an undue burden to one skilled in the pharmaceutical arts since there is inadequate guidance given to the skilled artisan, regarding the pharmaceutical use, for the reasons stated above.

Thus, factors such as "sufficient working examples", "the level of skill in the art" and "predictability", etc. have been demonstrated to be sufficiently lacking in the instant case for the instant method claims. In view of the breadth of the claims, the chemical nature of the invention, the unpredictability of receptor-ligand interactions in general, and the lack of working examples regarding the activity of the claimed compounds towards preventing Pneumocystis carinii infection and lack of any evidence that all immune-compromised mammals and all those with autoimmune diseases and disorders would be susceptible to Pneumocystis carinii infection, one having ordinary skill in the art would have to undergo an undue amount of experimentation to use the instantly claimed invention commensurate in scope with the claims.

MPEP 2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. In re Wright,

999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly justified here. Thus, undue experimentation will be required to make Applicants' invention.

Allowable Subject Matter

Claim 38, 39 and 41-43 are allowed.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM.

The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661.

The fax phone number for the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you

have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

Venkataraman Balasubramanian

9/25/2006